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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/826,302 | 04/19/2004 | Chun Li | 077319-0406 | 1314 |

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| EXAMINER | |
|---|---|
| DELACROIX MUIRHEI, CYBILLE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1614 | |

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/826,302 | LI ET AL. | |
| | Examiner | Art Unit | |
| | Cybille Delacroix-Muirheid | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *15-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RD

## *Detailed Action*

The following is responsive to applicant's amendment received Jan. 21, 2005.

Claims 1-14 are cancelled. No new claims are added. Claims 15-39 are currently pending.

Applicant's references submitted along with the amendment have been considered. However, the examiner respectfully requests that applicant submit a supplemental 1449 so that the examiner may initial the relevant citations and the references can be made of record.

The previous rejection of claim 31, under 35 USC 112, second paragraph, set forth in paragraph 1 of the office action mailed Oct. 1, 2004 is withdrawn in view of Applicant's amendment and the remarks contained therein.

The previous rejection of claims 15-39 under 35 USC 101 (double patenting) set forth in paragraph 2 of the office action mailed Oct. 1, 2004 is withdrawn in view of Applicant's amendment and the remarks contained therein. However, applicant's amendment necessitates the following new ground(s) of rejection under the judicially created doctrine of obviousness-type double patenting.

PLEASE NOTE: the obviousness-type double patenting rejections set forth in paragraphs 3-4 of the office action mailed Oct. 1, 2004 are maintained until receipt and approval of a terminal disclaimer.

## *New Ground(s) of Rejection*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 15-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,730,699. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and USPN '699 claim methods for treating cancer (lung, gastric, breast cancer, etc.) and enhancing the response of a tumor to irradiation, the methods comprising administering to a patient in need thereof an amount of a composition containing a taxoid compound such as paclitaxel, docetaxel, etoposide , etc. conjugated to a water-soluble polymer (20,000 to 80,000 daltons) and irradiating the tumor in order to treat the cancer or enhance tumor response. The water-soluble polymer may be polyglutamic acid.

The difference between the claims of the instant application and the claims of USPN '699 is that USPN '699 claims treatment of cancer or enhancement of tumor response using radiation in general, whereas the claims of the instant application specifically require the use of external radiation.

However, it would have been obvious to one of ordinary skill in the art to use external radiation in the claimed methods because claim 10 of USPN '699 requires the

use of gamma radiation, i.e. a type of external radiation. Thus, one of ordinary skill in the art would reasonably expect external radiation in combination with the taxoid conjugated water-soluble polymer compounds to successfully treat cancer or enhance tumor response.

***Claim Rejection(s)—35 USC 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 15-31, 35-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of a small group of specific cancers (see claim 32), does not reasonably provide enablement for treatment of all kinds of cancer embraced by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are

weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

**(1) The nature of the invention**:

The claims are drawn to a method for treating cancer in a patient, which comprises administering to the patient a (i) composition of a taxoid molecule conjugated to a water soluble polymer and (ii) external radiation.

**(2) The state of the prior art**

With respect to cancer, this a broad term which encompasses numerous forms of neoplastic diseases, each involving different types of tissues and organs and also includes blood-borne diseases. As recognized in the art, many different anti-neoplastic drugs are used to treat a variety of cancers, but there is no one drug or class of drugs, which is capable of treating all cancers in general. Please see pages 1226-1229 of Goodman & Gilman's.

**(3) The relative skill of those in the art**

The relative skill of those in the art is high. However, given the state of the art as set forth above, the artisan is currently unaware of any one particular anticancer agent or class of anticancer agents that is effective against all cancer cell types

**(4) The predictability or unpredictability of the art**

The unpredictability of the pharmaceutical and cancer art is high. Additionally, the lack of significant guidance from the present specification or prior art with regard to the actual treatment of all cancer cell types in a mammal, including a human, with the

claimed class of compounds as the active ingredient(s) makes practicing the claimed method unpredictable.

**(5) The breadth of the claims**

The complex nature of the subject matter to which the present claim is directed is exacerbated by the breadth of the claim. The claim is broad and encompasses treatment of a vast number of possible cancer types including solid tumors as well as blood-borne tumors.

**(6) The amount of direction or guidance presented**

Applicant's specification appears to only be enabled for the treatment of a limited number of cancers, such as ovarian, breast, hepatocarcinoma, lung cancer or fibrous sarcoma. It does not enable one of ordinary skill in the art to use the claimed invention in the treatment of the numerous neoplastic diseases covered by the term "cancer." Applicant's specification does not set forth a representative number of examples of cancers, which would be treated by the claimed compound.

**(7) The presence or absence of working examples**

The only working examples in the specification involve the use mice bearing ovarian carcinoma, mammary or breast (human), hepatocarcinoma or fibrous sarcoma cancer cell lines. Please see page 41, 44, 46, 49. The specification provides in vitro data using rat and human tumor cell lines, i.e. rat mammary tumor cell lines and human breast cancer cell lines, as well as cell lines resistant to paclitaxel. Please see pages 60-62.

**(8) The quantity of experimentation necessary**

Since the prior art recognizes that no one compound or class of compound(s) is capable of treating the vast number of possible cancerous diseases encompassed by the term "cancer"; (2) the specification shows anti-tumor activity only against a limited number of cancers, and (3) since the claims are very broad and include treatment of any type of cancer ranging from solid cancers to blood borne cancers, one of ordinary skill in the art would be burdened with undue experimentation to determine which cancers would be treated by administration of the claimed compound.

***Conclusion***

Claims 15-39 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Cybille Delacroix-Muirheid** whose telephone number is **571-272-0572**. The examiner can normally be reached on Mon-Thurs. from 8:30 to 6:00 as well as every other Friday from 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Christopher Low**, can be reached on **571-272-0951**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CDM
April 17, 2005

Cybille Delacroix-Muirheid
Patent Examiner Group 1600